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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/586,131	06/02/2000	Marc Delcourt	1184-00	6329

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SCHNADER HARRISON SEGAL & LEWIS, LLP
1600 MARKET STREET
SUITE 3600
PHILADELPHIA, PA 19103

EXAMINER	
FRIEND, TOMAS H F	

ART UNIT	PAPER NUMBER
1639	20

DATE MAILED: 04/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/586,131	Applicant(s) DELCOURT, MARC	
	Examiner Tomas Friend	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 12-20* is/are pending in the application.

4a) Of the above claim(s) *20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

Change of Art Unit Designation

Please note: The Art Unit location of this application in the PTO has changed from Art Unit 1627 to Art Unit 1639. To aid in matching papers to this application, all further correspondence regarding this application should be directed to **Group Art Unit 1639**.

Status of the Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 25 February 2003 has been entered.

The amendment received on 25 November 2002 (Paper no. 16) has been entered.

Status of the Claims

Claims 1-10 and 12-20 are pending in the present application. Claim 20 was withdrawn from further consideration in Paper No. 8. Claims 1-10 and 12-19 are examined on their merits.

Priority Claims

Acknowledgment is made of applicant's claim for foreign priority based on PCT/FR98/02629 and an application filed in France on 12 April 1997. It is noted, however, that applicant has not filed a certified copies of the PCT or the French application as required by 35 U.S.C. 119(b).

Withdrawn Rejections/Objections

All outstanding rejections and objections are withdrawn.

New Grounds of Rejection

The statutory basis for each of the following rejections not found below may be found in a prior office action.

New Grounds of Rejection - 35 U.S.C. 101

1. Claims 1-10 and 12-19 are rejected under 35 U.S.C. 101 for reasons made of record in Paper No. 8 (specific and substantial utility). This rejection was withdrawn in Paper No. 13 and is reintroduced in response to applicant's amendment in Paper No. 16.

Applicant argues that the claimed method is useful for screening to find sequences with enzymatic activity or homology to other sequences which can then be isolated, sequenced, or transfected and that the method has utility because the method can be used to isolate fragments with known utility (i.e. can be used to evaluate materials other than the screening method itself). Applicant argues the example of phenylketonuria or some other gene linked with enzyme deficiency supports the assertion that the claimed method has a specific and substantial utility.

Applicant's argument has been fully considered but it is not persuasive. Applicant must assert a specific and substantial utility at the time of filing. At the time of filing, applicant provided only the assertion that the method was useful for screening for finding sequences with enzymatic activity or homology to other sequences, which can then be isolated, sequenced, transfected. Applicant argues that the claimed method can be used to evaluate materials other than the screening method itself and therefor has utility. Applicant's claimed method is a method of isolating an intact clone of one target nucleic acid fragment having a known characteristic. No screening method steps are specified and no known characteristics are provided. Consequently, one wishing to use the claimed invention would not know what characteristic is being screened for or what method steps are involved in the screening. One may screen for a nucleic acid that shares a degree of homology with a known nucleic acid. The utility of the known nucleic, the degree of

homology being sought, the means of screening for a degree of homology, and any proposed correlation between the utility of the known nucleic acid and the isolated DNA which shares homology to the known nucleic acid are left to one using the invention to determine. In other words, the claimed method has not been developed to the point where a specific benefit to the public exists in the currently available form. The "real world" use of the presently claimed invention is not substantial because further research is required to identify and reasonably confirm a "real world" context of using the claimed method.

Applicant's specific example of phenylketonuria or some other gene linked with enzyme deficiency as a "real world" application of the claimed method was not provided in the application as filed and would not be a well established utility for the claimed invention. A "well established utility" is a "specific utility" which is well known, immediately apparent and implied by the specification based on the disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. The present disclosure, taken with the knowledge of a skilled artisan, would not make its application to phenylketonuria immediately apparent or imply its application to phenylketonuria. No "known characteristic" of a target nucleic acid related to a specified disease state is disclosed in the application nor is any application of the claimed method tat might be associated with a "known characteristic" exemplified.

New Grounds of Rejection – 35 U.S.C. 112, first paragraph

2. Claims 1-10 and 12-19 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

3. Claims 1-10 and 12-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The presently claimed invention is drawn to a process for isolating a clone of a nucleic acid fragment having a known characteristic from a group of nucleic acid fragments. The method steps include screening a group of monodigested nucleic acid libraries for a known characteristic.

The claimed process encompasses any known characteristic and any method of screening. Accordingly, the known characteristic includes, for example, a molecular weight, numbers and/or identities of restriction sites, any degree of homology to any other nucleic acid, the ability to encode any peptide or protein having any function including peptides that agonize or antagonize any receptor, activate or inhibit any enzyme, and treat any symptom of any disease. The scope "screening" encompassed by the present claims is even broader than the scope "known characteristic" because there is usually more than one assay for any given characteristic. For example, one may screen for a nucleic acid that encodes a peptide agonist of a receptor by expressing the peptide is a variety of different cell or phages and screen for binding to the receptor in solution or on a solid phase. One may also screen the same nucleic acid by expressing the peptide in a transgenic animal, in a transfected cell, or a transformed bacterium and assay for phenotypic changes associated with function of the target receptor. One may screen a nucleic acid for homology using solution phase assays, sandwich assays, and/or assays in which one or both of the test and target nucleic acids are bound to a solid phase, for example.

The present specification does not reasonably convey to one skilled in the art that the inventor, at the time the application was filed, had possession of the full scope of the claimed invention. Applicant has provided general descriptions of potential nucleic acid libraries, known characteristics, and some possible screening methods. Applicant's invention, however, is not drawn to a collection of nucleic acid libraries, known characteristics, and screening methods. Applicant's invention is drawn to a method in which a group of monodigested nucleic acid libraries is screened for a particular known characteristic and the library from which the group of monodigested libraries is made is digested with a plurality of restriction enzymes to isolate a single nucleic acid having the known characteristic. The specification does not describe or exemplify using the presently claimed process with even a single combination of library, known characteristic, and screening method step. Consequently, the present disclosure would not

reasonably convey to one skilled in the art that applicant, at the time of filing, had possession of the claimed process commensurate in scope with the claims.

4. Claims 1-10 and 12-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation (enablement).

This rejection appeared in Paper No. 8 and was withdrawn in Paper No. 13. Upon further consideration, the examiner introduces this rejection again and answers applicant's argument presented in Paper No. 10.

Several factors are to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any required experimentation is "undue." These factors include:

1) the breadth of the claims
2) the nature of the invention
3) the state of the prior art
4) the level of one of ordinary skill
5) the level of predictability in the art
6) the amount of direction provided by the inventor
7) the existence of working examples
8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The breadth of the claims is universal with regard to the nucleic acid fragments and associated characteristics encompassed by the claims. The fragments can be cDNA, genomic DNA, mitochondrial DNA, DNA derived form nature (from any organism), or synthetic DNA. The fragments may encode any protein or RNA having any function or be homologous to any other nucleic acid to any degree. All methods of screening for a characteristic of a nucleic acid fragment and/or its expression products are encompassed by the claims. These include Northern, Southern, and Western blots, ELISA, phage display and panning, binding assays, as well as any

assays for specific activities such as kinase activity and biological assays such as cell proliferation inhibition or disease treatments or cures.

The nature of the invention is a method for isolating an intact clone of one target nucleic acid fragment with a known characteristic from a group of fragments. The method involves restriction digests of cloned fragments to generate monodigested libraries that are screened for a known characteristic. The known characteristic will be present or absent depending on the whether the restriction enzyme used cleaves the fragment in such a way as to interfere with the known characteristic. The enzymes that do not interfere with the known characteristic are then used to cleave the source of the fragments to produce a multidigested library having one or more intact clones nucleic acid fragments from which a single intact clone is isolated.

The level of predictability in the art is low for circumstances in which the nucleic acid fragments and associated characteristics are not known. It is not possible to predict the outcome of screening, cloning, and restriction fragmentation when the characteristic being screened for and the nature of the nature and source of the nucleic acid are not specified in any way.

The amount of direction provided by the inventor is not adequate to enable one of ordinary skill in the art to use the claimed invention. No guidance as to nucleic acid selection, methods of screening, or characteristics to screen for is provided. No correlation is provided between any library, characteristic, and screening method. No working examples are provided to illustrate the use of the claimed method.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure is great. One using the invention must determine the characteristic to be screened for, the method(s) of screening, select a source(s) of target nucleic acid fragments, and make a cloning or cloning/expression vector that lacks restriction sites for 10 –70 different restriction enzymes and 3-4 other known restriction enzymes. Depending on the desired characteristics and nucleic acid fragments, expression vectors in bacteria, yeast, insects, plants, or animal cells or gene knockouts in mice or other animals or plants may be required to screen for the desired property.

For the reasons provided, undue experimentation would be required of one of ordinary skill in the art to use the claimed invention.

In Paper No. 10, applicant argues that [1] the skilled artisan using the claimed process will possess knowledge of the fragments of interest and the associated characteristic as evidenced by WO 97/27317 and US 6,261,782 and [2] there is no "magical relationship" between the number of examples (in the specification) and the breadth of the claims and no statutory requirement for working examples.

Applicant's arguments have been carefully considered but they are not persuasive. [1] Applicant's argument that the skilled artisan would possess knowledge of the fragments of interest and the associated characteristic is not supported by WO 97/27317 and US 6,261,782. The references cited by applicant do not disclose the presently claimed invention, do not include the same method steps, and are supported by completely different disclosures. Each application is examined on its own merits. Consequently, the argument that two references not cited in the present specification provide enablement for the presently claimed process is not persuasive. [2] The rejection of record does not state that a magical relationship exists between the number of working examples in the specification required for enablement and the breadth of the claims or that there is a statutory requirement for working examples. The rejection clearly states that a number of factors are to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any required experimentation is "undue." The factors considered as the grounds for the examiner's determination were presented in the rejection of record.

New Grounds of Rejection - 35 U.S.C. 112, second paragraph

5. Claims 1 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-10 and 12-19 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: method steps required to screen for a known characteristic (see, for example, claim 1, method step c). In the context of the present claims, screening in and of itself cannot be a single method step that would lead to the functional

linkage, for example, between method steps b and d of present claim 1. Elements of the screening method step required to provide results that would lead to the detection of intact fragments that can be related to the restriction enzymes used are not provided. Consequently, a gap currently exists between method steps b and d in claim 1.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Tomas Friend** at telephone number **(703) 308-4548**. The examiner's works on a flex-time schedule that may include Saturdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-2742.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist at (703) 308-1235.

Tomas Friend, Ph.D.
19 April 2003

ANDREW WANG
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600